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Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Abstracts from Invited Speakers

I-1
SIGNALING PATHWAYS IN CHONDROCYTE PATHOLOGY

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Purpose: Cartilage degeneration is one of the hallmarks of osteoarthritis (OA). Numerous studies have shown that changes in the behavior of cartilage cells (chondrocytes) themselves contribute to cartilage degeneration. Many signals including growth factors, cytokines and matrix fragments act on chondrocytes and control a plethora of intracellular signaling pathways. Our studies have identified the growth factor TGFalpha as a promoter of cartilage degeneration. The purpose of this study was to identify downstream signaling pathways and targets mediating TGFalpha effects on chondrocytes.
Methods: Mouse and rat models of OA were analyzed using histological and molecular approaches. These in vivo studies were complemented by cell and organ culture experiments using rat primary chondrocytes or cartilage explants cultured in the presence or absence of TGFalpha and modulators of downstream pathways. Outcome measures include gene and protein expression measured by qPCR and Western blotting.
Results: We identified the ERK1/2, RhoA/ROCK, p38 and PI3 K signaling pathways as main mediators of TGFalpha actions on chondrocytes. Amongst other responses, these pathways control the expression of the chemokine CCL2 and the endothelin A receptor, both of which contribute to the catabolic activities of TGFalpha.
Conclusions: TGFalpha induces a complex array of downstream signaling events leading to increased CCL2 and endothelin signaling that further promotes cartilage breakdown in OA.

I-2
CLINICAL RELEVANCE OF IMAGING IN OSTEOARTHRITIS – THE RADIOLOGIST'S PERSPECTIVE

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Imaging methods, especially magnetic resonance imaging (MRI), have been providing useful insights regarding the relationship between pathology in different structures of the joint and symptoms, as well as pathogenesis and progression of osteoarthritis. A variety of imaging methods is available and may be applied to assess qualitatively and quantitatively structures around the joint such as articular cartilage, subchondral bone, synovium, ligaments, and peri-articular soft-tissues. However, the choice of imaging methods and the use of adequate software and hardware are of utmost importance to properly evaluate each joint structure. MRI is the reference standard imaging method to assess different joint structures regarding osteoarthritis given its ability to manipulate contrast between different tissues, multiplanar capability, and high spatial resolution. Several reliable semiquantitative scoring systems have been applied to large observational studies and interventional clinical trials. Quantitative assessment is a powerful tool when changes occur homogeneously throughout large areas or structures in the joint. Compositional imaging has increased our ability to detect and monitor early degeneration before morphologic changes are present, which may help to prevent permanent structural changes commonly seen in OA. Optimization of the new available three-dimensional fast spin-echo sequences is of interest in osteoarthritis research since it may significantly reduce the time of acquisition while maintaining high resolution and quality imaging with spin-echo contrast. Ultrasound may play a role in monitoring inflammation affecting articular and peri-articular soft-tissues in osteoarthritis such as the synovium. Nuclear medicine and dynamic contrast-enhanced (DCE) MRI are potential tools to assess inflammation. Imaging became a major and relevant instrument for the understanding of genesis and progression of osteoarthritis, as well as for monitoring different therapies.

I-3
IMPLICATIONS OF CLINICAL BIOMECHANICS RESEARCH ON REHABILITATION FOR OA

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A growing focus of rehabilitation for OA is based on clinical biomechanics research, defined as the application of biomechanics to the treatment of patients. Clinical biomechanics can provide assistance with the identification of risk factors for disease and with the evaluation of interventions. Motion analysis laboratories capable of measuring three-dimensional kinematics and kinetics, often in combination with electromyography, have become a mainstay for evaluating a joint's dynamic, biomechanical environment. The vast majority of this research is directed towards the knee during walking, both because of the high prevalence of knee OA and because of the suitability of motion analysis laboratories for describing tibiofemoral joint loading. The external knee adduction moment receives particular attention in OA research and has important strengths and limitations regarding its relationship with internal knee joint loads and with the progression of disease. Although rehabilitation often targets biomechanics, it ultimately aims to improve pain, function and quality of life. Accordingly, the use of biomechanical measures as outcomes in clinical trials of rehabilitative interventions is perhaps their most promising, yet often disputed, application. For example, rehabilitative interventions intended to alter knee joint loads, and potentially disease progression, include: various functional strengthening and gait re-training methods focused on altering dynamic alignment; weight-loss; knee braces; footwear and orthotics; and gait aids. Abundant research suggests that many of these interventions can indeed decrease the knee adduction moment, although effect sizes range considerably, and what constitutes a clinically important change is unclear. When evaluated with randomized clinical trials using patient-important outcomes, the effectiveness of these interventions is much more variable. Exploring strategies that improve a joint's biomechanics is essential. Greater application to rehabilitation may rely on increased efforts to describe the clinical measurement properties of proposed biomechanical outcome measures, and on randomized clinical trials that evaluate changes in such measures in combination with other potential surrogate and patient-important outcomes.

I-4
INNOVATION IN MOLECULAR IMAGING WITH MASS SPECTROMETRY: RUNNING TOWARDS HIGH RESOLUTION

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The study of molecular signaling processes related to osteoarthritis requires not only the detection and analysis of the molecules involved but also the evaluation of their spatial organization. This allows the

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